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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/084,676	02/28/2002	Iris Ziegler	148/50932	2539

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EXAMINER	
FUBARA, BLESSING M	
ART UNIT	**PAPER NUMBER**
1618	

DATE MAILED: 11/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/084,676	ZIEGLER ET AL.	
	Examiner	Art Unit	
	Blessing M. Fubara	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17 and 38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of request for extension of time and request for continued examination under 37 CFR 1.114, declaration by Dr. Ziegler under 37 CFR 1.132 and remarks, all filed 10/27/05.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission filed on 10/27/05 has been entered.

Declaration under 37 CFR 1.132 by Dr. Ziegler

The production of applicants compound comprising tramadol HCl and diclofenac Na is carried out by homogeneously mixing the diclofenac Na and the tramadol HCl with microcrystalline cellulose in a Kenwood Chef mixer for 10 minutes and then granulated with water in an amount sufficient for moistening according to page 3 of the declaration.

The declaration also produces a mixture of diclofenac Na and tramadol HCl and auxiliary substances by screening the mixture through a screen and mixing in a blender for 10 minutes; after which the blended mixture was compressed on a Korsch EKO tablet press (page 2 of the declaration).

Then page 4 of the declaration provides release data for a) mixture of diclofenac and tramadol (test II, 75 mg and 50 mg and which is applicants invention) and b) individual tramadol at 75 mg and diclofenac at 50 mg. The declaration does not provide release data for the

suggested mixture of diclofenac and tramadol. The declaration does not also provide release data for the mixed product at page 2 of the declaration. The declaration is thus not persuasive.

Applicants' Remarks

Applicants state that Mauskop suggests a mixture of tramadol and diclofenac and that the suggested mixture differs from the claimed compound having a water solubility of $\leq$ 100 mg/ml; that Dr. Ziegler's declaration describes the difference between the mixture of Mauskop (Test 1) and the claimed compound (Test II).

Regarding claim 38, applicants argue that claim 38 requires repeated mixing and moistening steps and raises issue with Examiner's answer in the Final rejection to applicants' argument regarding cost.

2. Applicants' arguments filed 10/27/05 have been fully considered but they are not persuasive.

Test 1 of the declaration of Dr. Ziegler is directed to release of individual diclofenac and tramadol compositions and not to the suggested mixture of diclofenac and tramadol as Examiner describes above under DR. Ziegler's declaration. Examiner acknowledges applicants' recognition that Mauskop suggests mixture of tramadol and diclofenac.

Regarding the issue of the cost, Examiner was responding to applicants' argument regarding cost in the final rejection.

The oral formulation of Mauskop is discrete units such as capsules, cachets or tablets, or granules. The instant claim 38 is a process that involves mixing and any process where two components are combined requires the mixing of the two components. *Regarding the issue of the added cost for the production, it is noted that applicants provided no cost amounts for a*

formulation that is formed by mixing without repeated process of mixing and one that is formed with repeated mixing step. The number of times the mixing is repeated may be arbitrary to the skilled artisan since the mixing process ensures that the mixing process brings the components into intimate contact with each other. *The cost for repeated mixing and moistening was not considered by applicants in the claims and by the prior art* and the skilled artisan is capable of determine how many times the mixing and moistening would be done to effect adequate mixing of the components of the formulation in order to produce the oral formulation.

Claim Rejections - 35 USC § 102

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claim 17 is rejected under 35 U.S.C. 102(e) as being anticipated by Mauskop (US 5,914,129).

Mauskop discloses magnesium containing analgesic oral composition for the treatment/alleviation of pain, and specifically migraine headache pain (abstract). Solid formulations of the composition are capsules, catchets or tablets and powder or granules; liquid formulations are solution or suspension in aqueous liquid or non-aqueous liquid and oil-in-water or water-in-oil emulsions', and solid formulation of tablet and capsules are preferred with tablet being the most preferred (column 6, lines 12-21). In a particular embodiment of Mauskop, the magnesium containing analgesic composition includes at least two different non-opioid analgesic agents, at least two different opioid analgesic agents or at least one non-opioid analgesic agent

and at least one opioid analgesic agent and it is believed that a combination of non-opioid analgesic agents or opioid analgesic agents or a combination of non-opioid and opioid analgesic agents act synergistically to relieve pain (column 3, lines 47-54). In the case where the pharmaceutical composition comprises a combination of a non-opioid analgesic agent and an opioid analgesic agent (claim 6),. the non-opioid analgesic agent of ibuprofen, naproxen and diclophenac (diclofenac sodium) are included in the list of non-opioid analgesic agents provided (claims 1-4, 6 and 15) and the opioid analgesic agents of tramadol is included in the list of opioid analgesic agents provided (claims 1, 4, 5, 6 and 17); specifically pharmaceutically acceptable salts such as the hydrochloride salt is employable (column 3, lines 10-14). Mauskop, in column 6, lines 18-31, discloses how the tablet is formulated. Mauskop discloses a combination of opioid analgesic and non-opioid analgesic to synergistically act to relieve pain (column 3, lines 47-54) and tramadol hydrochloride and diclofenac sodium are included in the list provided (column 3, lines 1, 8 and 12). The property of a composition is not separable from the composition and how a composition is made has no patentable weight in a composition/product claim. Instant claim 17 reads on a composition, which is a mixture of diclofenac sodium and tramadol hydrochloride.

According to MPEP 2112.01 [R-2], "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. And "when the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the

burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Furthermore, each of the tramadol hydrochloride and the diclofenac sodium are compounds in themselves. Limitations from the specification cannot be read into the claims, (see In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993)). The release of tramadol or diclofenac is a property of the composition or the compound. It is also noted that instant claim 17 does not recite specific amounts of the respective drugs in the composition that distinguishes the instant claim 17 from the disclosed composition of the prior art.

Claim Rejections - 35 USC § 103

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Claim 17 is rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Mauskop (US 5,914,129).

The anticipatory rejection is described above. In the alternative, claim 17 is rendered obvious by Mauskop since as applicants acknowledge, Mauskop suggests a mixture of tramadol and diclofenac. Therefore, it would have been obvious to one of ordinary skill in the art to prepare a mixture of diclofenac and tramadol according to the teaching of Mauskop. One having ordinary skill in the art would have been motivated to formulate diclofenac (an analgesic) with an opioid analgesic such as tramadol with the expectation that the added opioid would relieve severe pain (column 3, lines 41 and 42).

7. Claim 38 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mauskop (US 5,914,129).

Mauskop discloses a composition comprising tramadol and diclofenac and a method of preparing the composition. Mauskop in column 6, lines 11-31 discloses forming tablets by conventional method of compression and molding and specifically discloses that molded tablets can be optionally moistened with an inert liquid diluent. The instant method comprises a mixing of tramadol hydrochloride and diclofenac sodium, which the prior art discloses/suggests. The instant method comprises a moistening step which the prior art discloses. Repeating the mixing and moistening steps is an obvious variant of the method at the disposal of the person of ordinary skill in the art or to the skilled artisan whereby the steps are repeated as necessary for the production of the desired tablet. Mauskop does not specifically disclose formulating the mixture under energy input. However, compressing or granulating the mixture requires some form of energy input (see the eighteenth edition of Remington's Pharmaceutical Sciences, 1990, pages 1641- 1 647 as a teaching reference in the compression and granulation of pharmaceutical preparations). However, a method of making compositions are disclosed and taught in the eighteenth edition of Remington's Pharmaceutical Sciences. Remington specifically teaches wet-granulation method, fluid-bed granulation method, dry-granulation method, direct compression and related granulation processes (pages 1641-1647). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to formulate the preparation of Mauskop by mixing and moistening the mixture as disclosed by Mauskop. One having ordinary skill in the art would have been motivated to apply the necessary energy to the mixture with the expectation of producing tablets.

Double Patenting

The provisional rejection of claim 17 remain under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 11 of copending Application No. 10/016,130 is withdrawn because the co-pending application is abandoned.

Therefore, applicants' argument with respect to the provisional obviousness type double patenting rejection is moot in light of the withdrawal of the rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 3:30 p.m. (Monday to Friday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Blessing Fubara
Patent Examiner
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